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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/898,750	WETMUR ET AL.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *117-178* is/are pending in the application.

4a) Of the above claim(s) *126,133,138,139, 142,143 and 149-178* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *117-125,127-132,134-137,140,141,144-148,179 and 180* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE and the amendment filed on May 15, 2009 have been entered. The claims pending in this application are claims 117-180 wherein claims 126, 133, 138, 142, 143, and 149-178 have been withdrawn due to restriction and species election requirements mailed on August 17, 2005. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of applicant's amendment filed on May 15, 2009.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. New Matter

Claims 117-125, 127-132, 134-137, 140, 141, 144-148, 179, and 180 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitation "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell" are added to the newly amended independent claim 117. Although the specification describes that "our single stranded displacers are not hybridized to a linker strand and are capable of initialing triplex formation at a point other than at the end of a recipient polynucleotide" (see page 16, lines 30-33), "[O]ne of the significant uses of our invention is for the site specific addition or deletion of nucleotides in a recipient polydeoxynucleotide sequence. This process occurs when the new strand is introduced to the recipient duplex and displaces the original strand" (page 19, lines 19-22), and the formation of a triplex displacer complex formed by a displacer and a recipient polynucleotide, page 16, line 31, page 19, lines 17-24, and Examples 13 and 14 of specification suggested by applicant do not describe such claim limitation because the nucleotides or nucleotide sequences of the recipient polynucleotide duplex are in the triplex displacer complex and has not be replaced, and has not be changed. Furthermore, nowhere in the specification describes that a triplex displacer complex formed by said displacer and said recipient polynucleotide complex is within a cell as recited in the claim. Therefore, there is a new matter in claim 117.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST

PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

Response to Arguments

In page 11, third paragraph bridging to page 13, last paragraph of applicant's remarks, applicant argues that page 16, line 31, page 19, lines 17-24, and Examples 13 and 14 of specification describe the limitation "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell" recited in claim 117.

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. Although the specification describes that "our single stranded displacers are not hybridized to a linker strand and are capable of initialing triplex formation at a point other than at the end of a recipient polynucleotide" (see page 16, lines 30-33), "[O]ne of the significant uses of our invention is for the site specific addition or deletion of nucleotides in a recipient polydeoxynucleotide sequence. This process occurs when the new strand is introduced to the recipient duplex and displaces the original strand" (page 19, lines 19-22), and the formation of a triplex displacer complex formed by a displacer and a recipient polynucleotide, page 16, line 31, page 19, lines 17-24, and Examples 13 and 14 of specification suggested by applicant do not describe such claim limitation because the nucleotides or nucleotide sequences of the recipient polynucleotide duplex are in the triplex displacer complex and has not be replaced, and has not be changed. Furthermore, nowhere in the specification describes that a

triplex displacer complex formed by said displacer and said recipient polynucleotide complex is within a cell as recited in the claim.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 117-125, 127-132, 134-137, 140, 141, 144-148, 179, and 180 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 117 is rejected as vague and indefinite in view of the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell". Since the claim requires that the displacer and the recipient polynucleotide duplex form a triplex displacer complex comprising the displacer and the recipient polynucleotide duplex, the nucleotides or nucleotide sequences of the recipient polynucleotide duplex are in the triplex displacer complex and has not be replaced, and has not be changed, it is unclear why said displacer can change at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex. Furthermore, since the claim does not require that a triplex displacer complex is formed in a cell or is transformed or transfected into a cell, it is unclear why said complex is within a cell. Please clarify.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 117-119, 121, 125, 134-136, 144, 145, 179, and 180 are rejected under 35 U.S.C. 102(e) as being anticipated by Lin et al., (US Patent No. 5,214,136, filed on February 20, 1990).

Regarding claim 117, Lin *et al.,* teach a nucleic acid displacer composition comprising an isolated oligo-or polynucleotide displacer (ie., 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4), said oligo- or polynucleotide displacer comprising two or more sequences: a) at least one first sequence (ie., CCC-TCT in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4) which complexes with said recipient polynucleotide duplex through triplex strand formation; b) at least one second sequence (ie., TT-TTT in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4), said second sequence being complementary to at least a portion of one strand of said recipient polynucleotide duplex and being base-paired with said portion, comprising one or more modified nucleotides (ie., CP in 3' of 5'-P-CCC-TCT-TTT-TTT-CCP) that increase stability; and comprising one or more nucleotides that form a mismatch (ie., T in 6 position in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4) with said strand of the recipient polynucleotide duplex as recited in the claim (see columns 8-10 and Table 4). Since the nucleic acid displacer taught by Lin *et al.,* has an ability to change at

least one nucleotide or a nucleotide sequence in a recipient polynucleotide duplex which is available in nature when the displacer is introduced to the recipient polynucleotide duplex, the recipient polynucleotide duplex and the triplex displacer-recipient complex recited in the claim are not parts of a nucleic acid displacer composition, and the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell" is not a structural limitation of the claim but is a functional limitation of the claim, Lin *et al.,* teach that said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell as recited in the claim.

Regarding claims 118, 119, and 121, Lin *et al.,* teach that said second sequence is adjacent to said first sequence as recited in claim 118 wherein said second sequence is separated from said first sequence by from 1 to 5 intervening moieties (ie., T in 6 position in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4) as recited in claim 119 and said intervening moieties are nucleotides as recited in claim 121 (see columns 8-10 and Table 4).

Regarding claim 125, Lin *et al.,* teach that least one of said nucleotides complementary to said strand of the recipient polynucleotide duplex is modified to increase the stability of the displacer-recipient complex, wherein the modification is in the second sequence (ie., CP in 3' of 5'-P-CCC-TCT-TTT-TTT-CCP) (see columns 8-10 and Table 4).

Regarding claims 134-136, since Lin *et al.,* teach that 5'-P-CCC-TCT-TTT-TTT-CCP is resistant to snake venom phosphodiesterase digestion, it is known that snake venom phosphodiesterase is an exonuclease (see page 1 of attachment for snake venom phosphodiesterase), and claim 134 does not require that at least one moiety attached to a terminus of the oligo or polynucleotide is different from the one modified nucleotide recited in claim 117, Lin *et al.,* disclose at least one moiety attached to a terminus of the oligo or polynucleotide, said moiety conferring exonuclease resistance to the terminus to which it is attached as recited in claim 134 wherein said moiety is attached to a terminal nucleotide (ie., anthraquinone of P in 3' of 5'-P-CCC-TCT-TTT-TTT-CCP) as recited in claim 135 and said moiety is indirectly attached to a terminal nucleotide as recited in claim 136 (ie., by P in 3' of 5'-P-CCC-TCT-TTT-TTT-CCP) (see columns 8-10 and Table 4).

Regarding claims 144 and 145, Lin *et al.,* teach further comprising a modification (ie., a fluorescent label) which permits detection of the displacer-recipient complex as recited in claim 144 wherein said modification comprises a member selected from the group consisting of non-radioactive labels, radioactive labels, fluorescent labels, chemiluminescent labels, enzymes and targets for detection as recited in claim 145 (see column 5, lines 51-64).

Regarding claim 179, since the recipient polynucleotide duplex recited in the claim is not a part of a nucleic acid displacer composition and the nucleic acid displacer taught by Lin *et al.,* has an ability to changes at least one nucleotide or a nucleotide sequence in a recipient polynucleotide duplex which is available in nature, claim 179 is anticipated by Lin *et al.*.

Regarding claim 180, since the claim does not require that the oligo-or polynucleotide displacer is a duplex, Lin *et al.,* teach that the ligo-or polynucleotide displacer comprises a

displacer strand (ie., CCC-TCT in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4) and a linker strand (ie., TTT-TTT-CCP in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4) as recited in claim 180.

Therefore, Lin *et al.,* teach all limitations recited in claims 117-119, 121, 125, 134-136, 144, 145, 179, and 180.

Response to Arguments

In page 12, last paragraph bridging to page 13, last paragraph of applicant's remarks, applicant argues that: (1) "[L]in describes a displacer which binds or complexes with a duplex. The strand that is purported to be a displacer (which will be referred to as 'LD' for Lin's Displacer) is a polyprimidine which is used in a stability assay. The LD hybridizes to its complementary strand ('LC' for Lin's Complement). Although this complementary sequence (LC) is not specified, its sequence may be ascertained from the sequence of LD. Applicants explained in the previously submitted response that Lin does not describe triple strand formation, but rather only refers to normal hybridization of a sequence to its complement"; and (2) in view of LD1 (5' P-CCC-TCT-TTT-TTT-CCP 3'), LC (3' GGG-AGA-AAA-AAA-GG 5'), and LD2 (3''PCC-TTT-TTT-TCTCCC-P 5' LD2), Lin *et al.,* do not teach that the second sequence of the nucleic acid displacer recited in claim 117 because the first sequence of the displacer such as LD2 can bind to the recipient polynucleotide through triplet strand formation by parallel binding and the second sequence of the displacer such as LD2 cannot bind to the recipient polynucleotide by normal Watson-Crick base pairing which occurs through an anti-parallel orientation.

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although Lin *et al.,* do not directly teach changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide duplex of a triplex displacer

complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell, since the nucleic acid displacer taught by Lin *et al.,* has an ability to change at least one nucleotide or a nucleotide sequence in the recipient polynucleotide duplex which is available in nature when the displacer is introduced to the recipient polynucleotide duplex, the recipient polynucleotide duplex and the displacer-recipient complex recited in claim 117 are not parts of a nucleic acid displacer composition, and the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell" recited in claim 117 is not a structural limitation of the claim but is a functional limitation of the claim, Lin *et al.,* do teach that said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell as recited in claim 117. Second, the office action does not indicate that the duplex formed by LD1 (5' P-CCC-TCT-TTT-TTT-CCP 3') and LC (3' GGG-AGA-AAA-AAA-GG 5') is the recipient polynucleotide duplex argued by applicant. Third, applicant has no evidence to show that TT-TTT in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4 of Lin et al., cannot serve as the second sequence of the displacer recited in claim 117 and cannot bind to a recipient polynucleotide duplex which is available in nature by normal Watson-Crick base pairing which occurs through an anti-parallel orientation. Fourth, claim 117 does not require that the second sequence of the displacer binds to a recipient

polynucleotide duplex by normal Watson-Crick base pairing which occurs through an anti-parallel orientation as argued by applicant.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 146 and 147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.,* as applied to claims 117-119, 121, 125, 134-136, 144, 145, 179, and 180 above, and further in view of Dattagupta *et al.,* (US Patent No. 4,737,454, published on April 12, 1988).

The teachings of Lin *et al.,* have been summarized previously, *supra*.

Lin *et al.,* do not disclose that said modification in claim 144 is selected from the group consisting of biotin moieties, phosphorothioate linkages and antigens as recited in claim 146 and

a modification which allows capture of the displacer-recipient complex by affinity chromatography as recited in claim 147.

Regarding claims 146 and 147, Since Dattagupta *et al.,* teach that a nucleic acid probe can be labeled with hapten or biotin, an enzyme such as a β-galactosidase or horse radish peroxidase, a fluorescent radical, a phycobiliprotein, a luminescent radical, or a radioisotope (see abstract) and it is known that biotin binds to avidin, Dattagupta *et al.,* disclose that said modification (ie., biotin) in claim 144 is selected from the group consisting of biotin moieties, phosphorothioate linkages and antigens as recited in claim 146 and a modification which allows capture of the displacer-recipient complex by affinity chromatography (ie., the affinity chromatography comprising avidin) as recited in claim 147.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made the displacer recited in claims 146 and 147 wherein said modification is biotin moieties and the modification (ie., biotin) which allows capture of the displacer-recipient complex by affinity chromatography (ie., the affinity chromatography comprising avidin) in view of the prior art of Lin *et al.,* and Dattagupta *et al.*. One having ordinary skill in the art would have been motivated to do so because the simple replacement of one kind of label (ie., the fluorescent label taught by Lin *et al.,* see column 5, lines 51-64) from another kind of label (ie., the biotin label taught by Dattagupta *et al.,*) during the process of labeling the displacer recited in claims 146 and 147, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the label taught by Lin *et al.,* and the label taught by Dattagupta *et al.,* are used for the same purpose (ie., labeling a nucleic acid probe).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

In page 16, third paragraph bridging to page 17, second paragraph of applicant's remarks, applicant argues that "[A]s explained in detail above, Lin does not describe triple strand formation as currently claimed. Dattagupta does not cure the deficiencies of Lin. Like Lin, Dattagupta teaches only single stranded recipient molecules. The combination of Lin and Dattagupta do not result in the presently claimed invention of a nucleic acid displacer composition which binds with a recipient polynucleotide duplex through triplex strand formation. The references do not render the claims obvious because a person of ordinary skill in the art would have no motivation to combine the references, nor an expectation of success in the combination, because neither reference teaches triplex strand formation".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although Lin *et al.,* do not directly teach changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell as recited

in claim 117, since the nucleic acid displacer taught by Lin *et al.,* has an ability to change at least one nucleotide or a nucleotide sequence in the recipient polynucleotide duplex which is available in nature when the displacer is introduced to the recipient polynucleotide duplex, the recipient polynucleotide duplex and the triplex displacer-recipient complex recited in claim 117 are not parts of a nucleic acid displacer composition, and the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell" recited in claim 117 is not a structural limitation of the claim but is a functional limitation of the claim, Lin *et al.,* do teach that said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell as recited in claim 117. Second, triplex strand formation is not a structural limitation recited in claim 117. Third, there is a motivation for combining Lin *et al.,* and Dattagupta *et al.,* together (see above office action).

11. Claim 148 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.,* as applied to claims 117-119, 121, 125, and 134-136 above.

The teachings of Lin *et al.,* have been summarized previously, *supra*.

Lin *et al.,* do not disclose an artificially constructed polynucleotide hybrid comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition of claim 118 as recited in claim 148.

However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made an artificially constructed polynucleotide hybrid comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition of claim 118 as recited in claim 148 by hybridizing the nucleic acid displacer composition of claim 118 to a naturally occurring double stranded DNA. One having ordinary skill in the art would have been motivated to do so because Lin *et al.,* have tested the stabilities of the oligonucleotides coupled to anthraquinone *in vitro* and *in vivo* (see column 7, lines 49-51) and oligonucleotide sequences modified by conjugation to at least one unsubstituted or substituted anthraquinone at other than the 5' terminus have favorable properties in enhancing hybridization to target DNA or RNA without loss of specificity and show enhanced stability to nucleases (see abstract) and one having ordinary skill in the art would select a naturally occurring recipient polynucleotide duplex such as a naturally occurring double stranded DNA for making the artificially constructed polynucleotide hybrid recited in claim 148 based on his or her experimental requirements. One having ordinary skill in the art at the time the invention was made would have a reasonable expectation of success to make an artificially constructed polynucleotide hybrid comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition of claim 118 as recited in claim 148 by hybridizing the nucleic acid displacer composition of claim 118 to a naturally occurring double stranded DNA.

Response to Arguments

In page 17, third paragraphs bridging to page 18, first paragraph of applicant's remarks, applicant argues that "[L]in does not teach a nucleic acid displacer composition which binds with

a recipient polynucleotide duplex through triplex strand formation, a structural component required by claim 117 (from which claim 148 ultimately depends). A person of ordinary skill in the art would have no motivation to alter the teaching of Lin because, as explained above, it is extremely unlikely that the suggested TT-TTT segment will have the ability to bend sufficiently to hybridize with its complementary segment in the LC strand. Such an event would be so energetically unfavorable that there would be no reasonable expectation of success. Claim 148 is not obvious over Lin".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although Lin *et al.,* do not directly teach changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell, since the nucleic acid displacer taught by Lin *et al.,* has an ability to change at least one nucleotide or a nucleotide sequence in the recipient polynucleotide duplex which is available in nature when the displacer is introduced to the recipient polynucleotide duplex, the recipient polynucleotide duplex and the displacer-recipient complex recited in claim 117 are not parts of a nucleic acid displacer composition, and the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell" recited in claim 117 is not a structural limitation of the claim but is a functional limitation of the claim, Lin *et al.,* do teach that said displacer changes at least one nucleotide or a nucleotide sequence in said

recipient polynucleotide duplex of a triplex displacer complex formed by said displacer and said recipient polynucleotide complex when the displacer is introduced to the recipient polynucleotide duplex and said complex is within a cell as recited in claim 117. Second, the office action does not indicate that the duplex formed by LD1 (5' P-CCC-TCT-TTT-TTT-CCP 3') and LC (3' GGG-AGA-AAA-AAA-GG 5') is the recipient polynucleotide duplex argued by applicant. Third, applicant has no evidence to show that TT-TTT in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4 of Lin et al., cannot serve as the second sequence of the displacer recited in claim 117 and cannot bind to a recipient polynucleotide duplex which is available in nature by normal Watson-Crick base pairing which occurs through an anti-parallel orientation. Fourth, claim 117 does not require that the second sequence of the displacer binds to a recipient polynucleotide duplex by normal Watson-Crick base pairing which occurs through an anti-parallel orientation as argued by applicant. Fifth, there is a motivation for rejecting claim 148 (see above office action).

Conclusion

12. No claim is allowed.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz, can be reached on (571)272-0763.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /
Primary Examiner, Art Unit 1634
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